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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/506,327	09/02/2004	Shingo Hiramatsu	0210-0190PUS1	1247
2292 7590 01/08/2009 BIRCH STEWART KOLASCH & BIRCH PO BOX 747 FALLS CHURCH, VA 22040-0747			EXAMINER SAJJADI, FERAYDOUN GHOTB	
			ART UNIT 1633	PAPER NUMBER
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mailroom@bskb.com

Office Action Summary	Application No.	Applicant(s)	
	10/506,327	HIRAMATSU ET AL.	
	Examiner	Art Unit	
	FEREYDOUN G. SAJJADI	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 29 September 2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-21,23,24,26-28 and 30-45 is/are pending in the application.
- 4a) Of the above claim(s) 1-20,40 and 41 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 21,23,24,26-28,30-39 and 42-45 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>10/22/2008 and 10/31/2008</u> . | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Status

Applicants' response dated September 29, 2008, to the non-final action dated June 27, 2008, has been entered. Claim 22 has been cancelled, and claims 21, 23, 27, 30-32 and 38 amended. No claims were newly added. Accordingly, claims 1-21, 23, 24, 26-28 and 30-45 are pending in the application. Claims 1-20, 40, and 41 remain withdrawn from further consideration, with traverse. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Claims 21, 23, 24, 26-28, 30-39 and 42-45 are under current examination.

Information Disclosure Statement

The information disclosure statement filed 10/22/2008 is not compliant with 37 CFR 1.98(a)(2), as the references contained therein are in the Japanese language. The information disclosure statement filed 10/31/2008 containing an English translation of the Japanese references has been considered, and indicated as such on form PTOSB/08b.

Response to Claim Objections

Claims 21-23 were objected to for claiming nucleotide sequences considered essential subject matter by reference to nucleotides 57444 to 62927 of GenBank Accession No. AF226688, and further not in compliance with 37 CFR 1.57 and 37 CFR 1.821-1.825, in the previous office action dated June 27, 2008. Applicants' cancellation of claim 22 renders its objection moot.

In view of Applicants' amendment of claims 21 to 23 to recite nucleotides 1 to 5484 of SEQ ID NO: 23 (that correspond to nucleotides 57444 to 62927 of GenBank Accession No. AF 226688), obviating the ground of objection, the previous objection is hereby withdrawn.

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Response to Claim Rejections - 35 USC § 112- New Matter

Claim 21-23 were rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement and introducing new matter in the previous office action dated June 27, 2008. Applicants' cancellation of claim 22 renders its rejection moot.

In view of Applicants' amendment of claims 21 to 23 to recite nucleotides 1 to 5484 of SEQ ID NO: 23, and deleting language referring to a fibroin H chain gene promoter positioned in tandem with the recited sequence, the previous rejection is hereby withdrawn.

Response & Maintained Claim Rejections - 35 USC § 103

Claims 21-24, 26-28, 30-39 and 42-45 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Liu et al., US 2002/0137211 in view of Zhao et al. (Acta Biochimica et Biophysica Sinica 33(1): 112-116, Jan. 2001); Zhang et al. (Acta Biochimica et Biophysica Sinica 31(2): 119-123, 1999) and GenBank Acc. No. AF226688. Applicants' cancellation of claim 22 renders its rejection moot. The rejection set forth on pp. 4-8 of the office action dated October 31, 2007, and pp. 4-5 of the previous office action dated June 27, 2008 is maintained for claims 21, 23, 24, 26-28, 30-39 and 42-45, for the reasons of record.

Applicants traverse the rejection, and with reference to MPEP §2143, argue that the *Graham v. Deere* factual inquiries have not been resolved, because no rationale has been provided for determining obviousness, and the present invention is distinct from the cited references, as the gene cassette of the present invention contains a sequence enhancing an activity of a fibroin H chain promoter and a sequence enhancing an expression of an exogenous gene under the control by the fibroin H chain promoter. Applicants' arguments have been fully considered, but are not found persuasive.

The rejection previously set forth indicated that nucleotides 57444 to 62927 of GenBank Accession No. AF 226688 corresponds to nucleotides 1 to 5484 of SEQ ID NO: 23, previously examined in rejected claim 26. Zhao discloses a transgenic silkworm with a genome comprising a "gene cassette" embraced by the instant claims. The gene cassette comprises, in order, the 5' end of the endogenous fibroin H-chain gene, including the promoter. The structural organization and sequence of the *Bombyx mori* fibroin heavy chain gene and its promoter was known in the prior art as GenBank Accession No. AF 226688. The language of instant claim 21, part (2) is

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open and is therefore inclusive of sequences 1-5484 of SEQ ID NO:23; thus not precluding additional sequences that are part of SEQ ID NO: 23, or GenBank Accession No. AF 226688. Therefore, a person of ordinary skill in the art having utilized the promoter sequences of GenBank Accession No. AF 226688 in a gene cassette, would necessarily include nucleotides 1-5484 of SEQ ID NO: 23. As the instant claims do not limit any sequences to only those of 1-5484, the issue of motivation to limit the promoter to only the recited sequences is moot.

Applicants argue that the gene cassette disclosed in the Liu reference uses fibroin L chain (not H chain as in the present invention), and does not describe or suggest the above-mentioned features of the present invention. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). There is no requirement for Liu et al. to disclose each and every limitation of the claim in an obviousness rejection, based on the teachings of a plurality of references. Liu et al. teach an alternative method, providing a design choice to a person of ordinary skill in the art for introducing a transgene into *Bombyx mori*, to express a heterologous protein. Said design choice amounting to combining prior art elements according to known methods to yield predictable results.

Applicants argue Zhao and Zhang do not describe or suggest that the sequence in question has a function for enhancing expression of an exogenous gene in the silk gland. Additionally, the gene cassette of Zhao and Zhang does not contain a region enhancing the expression of promoter activity, upstream of the fibroin H chain promoter. Such is not found persuasive, because it is noted that the features upon which applicant relies (i.e., sequences for enhancing promoter activity) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

As previously indicated on the record, Zhao discloses a transgenic silkworm with a genome comprising a "gene cassette" embraced by the instant claims. The gene cassette comprises, in order, the 5' end of the endogenous fibroin H-chain gene, including the promoter, exon 1, intron I, and the 5' end of exon II terminated by a PstI site, fused in-frame to a GFP coding sequence, fused in frame to coding sequence for a synthetic fibroin like sequence, fused

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in frame to a 3' terminal portion of the endogenous fibroin H-chain gene, comprising the three Cys residues, and the endogenous genomic sequence flanking the 3' end of the Fib-H coding sequence, that was introduced into the gene targeting vector of Zhang et al.

Applicants argue that in the transgenic silkworm construction system using piggyBac transposon described in the Liu reference and the gene cassette described in the Zhao and Zhang references, there is a level of unpredictability that a skilled artisan would not be able to predict that a sequence of 5' terminal side of the fibroin H chain gene is essential for enhanced expression of an exogenous gene. Such is not found persuasive, because as already indicated, the instant claims fail to limit the promoter sequences to only an expression enhancing region.

Citing *KSR Int'l Co. v Teleflex Inc.*, 82 USPQ2d 1385 (U.S. 2007) and the TSM test, Applicants argue that There is no disclosure within the cited references that would lead the biochemist/biologist to identify the upstream region of the fibroin H chain promoter, which enhances the expression of an exogenous gene in the silk gland on the basis of genomic sequence information, from an infinite set of sequences. Such is not found persuasive, because the sequence of the fibroin H promoter disclosed as GenBank AF226688 does not constitute an infinite sequence. Moreover, the KSR case does not limit an obviousness rejection to a strict TSM test, as the KSR case forecloses the argument that a **specific** teaching, suggestion, or motivation is required to support a finding of obviousness See the recent Board decision *Ex parte Smith*, --USPQ2d--, slip op. at 20, (Bd. Pat. App. & Interf. June 25, 2007) (citing KSR, 82 USPQ2d at 1396) (available at <http://www.uspto.gov/web/offices/dcom/bpai/prec/fd071925.pdf>). In the instant case, a person of ordinary skill in the art is provided a design choice by the teachings of Zhao et al. and Liu et al. to utilize either the fibroin H chain or L chain sequences in the construction of a transgene expression vector, to make the analogous construct using the fibroin H-chain gene sequences in place of the L-chain gene sequences. Said design choice amounting to combining prior art elements according to known methods to yield predictable results, as silk fibroin is made up of both heavy and light chains, and one of skill in the art would recognize that the H-chain gene sequences and L-chain gene sequences were equivalents for producing transgenic silk.

Thus, the rejection of claims 21, 23, 24, 26-28, 30-39 and 42-45 is maintained, for reasons of record, and the foregoing commentary.

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Conclusion

Claims 21, 23, 24, 26-28, 30-39 and 42-45 are not allowed.

THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR§1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to FEREDOUN G. SAJJADI whose telephone number is (571)272-3311. The examiner can normally be reached on 6:30 AM-3:30 PM EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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/Fereydoun G Sajjadi/
Examiner, Art Unit 1633